EFFECTS OF d-AMPHETAMINE, COCAINE, AND PHENCYCLIDINE ON THE ACQUISITION OF RESPONSE SEQUENCES WITH AND WITHOUT STIMULUS FADING

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In each of three components of a multiple schedule, monkeys were required to emit a different sequence of four responses in a predetermined order on four levers. Sequence completions produced food on a fixed-ratio schedule. Errors produced a brief timeout. One component of the multiple schedule was a repeated-acquisition task where the four-response sequence changed each session (learning). The second component of the multiple schedule was also a repeated-acquisition task, but acquisition was supported through the use of a stimulus-fading procedure (faded learning). In a third component of the multiple schedule, the sequence of responses remained the same from session to session (performance). At higher doses, d-amphetamine, cocaine, and phencyclidine decreased the overall rate of responding and increased the percent errors in all three components. At lower doses, however, the three drugs produced selective effects on errors. Errors were increased in the learning component at lower doses than those required to disrupt the behavior in the faded-learning component. The performance component tended to be the least sensitive to disruptive drug effects. The data are consistent with the view that stimulus fading can modulate the effects of drugs on acquisition.

Key words: repeated acquisition, multiple schedule, stimulus fading, stimulus control, d-amphetamine, cocaine, phencyclidine, lever press, monkeys

The effects of several different stimulusfading procedures on the acquisition of complex discriminations have been studied using the technique of repeated acquisition (e.g., Boren, 1969; Sidman & Rosenberger, 1967). In these studies, monkeys were required to respond in a predetermined order on some number of operanda with a food reinforcer delivered at the end of the sequence. In each session, the subject was required to learn a different sequence of responses. Incorrect responses (e.g., pressing the left or right lever when the center lever was correct) produced a brief timeout. Over time, both the pattern of acquisition and the number of errors reached a steady state from session to session (cf. Boren, 1963; Boren & Devine, 1968). Using this type of baseline, Sidman and Rosenberger (1967) investigated the effects of a stimulus-fading procedure on the acquisition of serial response sequences. In that study the discriminative

stimulus for each correct response in the sequence was faded out sequentially, beginning with the response closest to reinforcement. They found that monkeys could acquire a longer sequence of responses with the fading procedure than without it. Boren (1969), using a procedure where all of the discriminative stimuli in the sequence to be acquired were faded simultaneously, obtained similar results.

The technique of repeated acquisition has also been found to be a sensitive method by which a drug's effect on "learning" may be studied. Experiments using a variety of drugs have shown that responding under an acquisition baseline is disrupted (e.g., errors are increased) at doses lower than those that disrupt a comparable performance baseline, where the discrimination is the same each session (Moerschbaecher, Boren, Schrot, & Simoes Fontes, 1979; Thompson, 1973, 1974, 1975, 1977; Thompson & Moerschbaecher, 1979). For example, Moerschbaecher et al. (1979) used a multiple schedule of repeated acquisition and performance of conditional discriminations to study the effects of cocaine and damphetamine in pigeons. They found that on both an acute and chronic basis, responding in the acquisition component was disrupted at

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doses that had little or no effect on responding in the performance component. Thompson and Moerschbaecher (1979) obtained similar results in monkeys responding under a multiple schedule of repeated acquisition and performance of response chains. One possible reason that an acquisition baseline is more sensitive to disruptive drug effects than a comparable performance baseline may be related to different conditions of stimulus control. The degree of stimulus control may function as a determinant of a drug's effect on behavior (see reviews by Laties, 1975; Thompson, 1978). Behavior under strong control by external stimuli is generally less affected by drugs than behavior under weak control by external stimuli.

Given that the acquisition of a discrimination can be modulated by a fading procedure and that the conditions of stimulus control can modulate the effects of drugs on behavior, it might be expected that a fading procedure would modulate the effects of drugs on acquisition. Inasmuch as there would be a stronger degree of stimulus control over behavior during acquisition with a fading procedure than without, the effects of a drug might be attenuated by the use of a fading procedure. The present study was therefore designed to determine how a fading procedure may modify the effects of three drugs, d-amphetamine, cocaine, and phencyclidine, on acquisition. A multiple schedule was used in order to permit a direct comparison, within the same session, of a drug's effect on acquisition with and without a fading procedure. To provide an additional comparison, a performance condition where the sequence of correct responses remained the same each session comprised the third component of the multiple schedule.

METHOD

Subjects

Two adult female patas monkeys served. Both subjects had experimental histories involving the repeated acquisition of behavioral chains. Each subject was maintained at about 85% of its free-feeding weight (5.75 and 6.2 kg) on a diet consisting of Noyes bananaflavored fool pellets, Purina Monkey Chow, fruit, and vitamins. The pellets were either earned during the experimental session or,

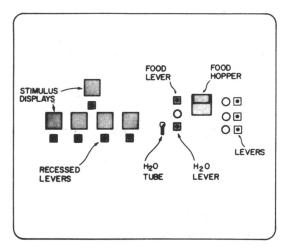


Fig. 1. Schematic of response panel that was mounted on each monkey's cage.

when necessary, provided after the session. Monkey chow, fruit, and vitamins were given to each subject after the daily session. Water was continuously available.

Apparatus

Each subject was housed in a primate cage (Research Equipment Co., model LC-1004) measuring 76.2 cm by 71.1 cm by 96.5 cm. The bars were removed from one side of the cage and replaced with an aluminum panel. The configuration of this panel is shown in Figure 1. An array of four recessed levers (C. P. Clare Co., model C10647) was aligned horizontally to the left of the vertical midline of the panel. The levers were spaced 4 cm apart, center to center, and were 45 cm above the cage floor. Each lever required a minimum force of .98 N for activation. A relay mounted behind the panel clicked when any one of the four levers was pressed. An in-line projector (BSR/LVE, model IC 901-696), mounted 4 cm above each lever, was used to project the different stimuli (colors). An additional lever, which operated the pellet dispenser, was mounted 11 cm to the right and 6 cm up from the center of the righthand lever. A green pilot lamp (no. 1820) was mounted 6 cm below the food lever. A pellet aperture (8 cm by 8 cm) was located 3 cm to the right from the center of the food lever. The remaining devices (i.e., levers, stimulus lamps, water dispenser) that were mounted on the panel were not used during the present experiment. Solid-state scheduling and recording equipment was located in an adjacent room.

Procedure

Baseline. The baseline procedure consisted of a three-component multiple schedule. In each component the subject was required to emit a different sequence of four responses in a predetermined order on the four recessed levers. A different stimulus (red, blue, or green) was projected above the levers during each component. Within a component, however, the stimulus over the levers did not change; i.e., there was a tandem four-response sequence in each component of the multiple schedule. Following each completion of the four-response sequence, the stimuli over the levers were turned off and the green pilot lamp under the food lever was illuminated. A press on the food lever then operated the pellet dispenser. The food-pellet reinforcer (500 mg), however, was delivered after every second completion of the sequence (i.e., responding was maintained under an FR 2 schedule). This was accomplished by simply plugging every other delivery hole in the dispenser. Following operation of the dispenser, the green pilot lamp was turned off, the sequence reset, and the stimuli above the four levers were turned on. When the monkey pressed an incorrect lever (e.g., a press on lever 2 when lever 4 was correct), the error produced a 5-sec timeout. During the timeout, all stimuli were off and responses had no scheduled consequences. An error did not reset the sequence.

Components of the multiple schedule changed after the completion of 40 sequences (20 reinforcements) or 20 min, whichever occurred first. A 5-sec blackout separated each component change. The components occurred in the following order each session: learning, performance, faded learning, learning, performance, faded learning, etc. A daily session terminated after 180 reinforcements or 4 hr, whichever occurred first.

In the performance component of the multiple schedule, the sequence of correct responses was the same each session: lever 3, lever 1, lever 2, lever 4; food under the FR 2 schedule. During this component the stimulus over each of the four levers was blue for Monkey C and red for Monkey F. In the learning component of the multiple schedule, the four-response sequence was changed from

session to session (repeated acquisition). During each session the monkey's task was to acquire a different four-response sequence by pressing the four levers in a particular order. For example, during one session the correct sequence of lever presses was 4-3-1-2, while during the next session the correct sequence was 3-2-4-1. The stimuli during this component were red for Monkey C and blue for Monkey F. The faded-learning component of the multiple schedule also consisted of a repeated-acquisition task, where the four-response sequence changed each session. Acquisition in this component, however, was supported through the use of a stimulus-fading procedure. In the first step of the fading procedure, only the stimulus lamp over the correct lever was fully illuminated at each sequence position, while the lamps over the incorrect levers were off. In subsequent steps the luminance levels of the lamps over the incorrect levers increased, until at the final step the lamps over all four levers were fully illuminated. There was a total of eight steps in the stimulus-fading procedure which titrated under the following conditions: Completion of a correct sequence advanced the fading level one step; every fourth error within a single sequence decreased the fading level one step. A component change did not affect the fading level. For example, if the subject finished the first faded-learning component at step five, the next faded-learning component would resume with the fading level at step five.

For each of the two acquisition components, different sequences were carefully selected to be equivalent in several ways and there were restrictions on their ordering across sessions (cf. Thompson, 1973). In each sequence each of the four levers was used once. Between the two acquisition components there were also restrictions on the sequences which were used. First, during any given session the same lever did not appear in the same sequence position in the two components. Second, a given sequence was assigned to either the learning or faded-learning component and never appeared in the alternate component during drug testing. Examples of the sequences used in each component for six consecutive sessions are shown in Table 1.

The data for each session were analyzed in terms of (a) the overall response rate (total responses/min, excluding timeouts) in each

Table 1

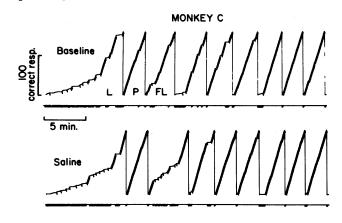
An example of sequences used in six consecutive sessions for each of the two acquisition components of the multiple schedule.

Consecutive sessions	Schedule components	
	Faded learning	Learning
1	1-2-4-3	4-3-1-2
2	2-1-3-4	3-2-4-1
3	3-4-1-2	1-3-2-4
4	4-3-2-1	3-1-4-2
5	3-2-1-4	2-4-3-1
6	1-3-4-2	4-1-2-3

component and (b) the overall accuracy or percent errors [(errors/total responses) \times 100] in each component. In addition to these measures based on session totals, within-session changes in responding were monitored by a

cumulative recorder. For example, acquisition of the response sequence in each learning component was indicated by within-session error reduction.

Drug testing. Before the drug testing began, the multiple-schedule baseline was stabilized. The baseline was considered stable when the response rate and percent errors in each component no longer showed systematic change from session to session. After baseline stabilization (60 to 70 sessions), dose-effect data were obtained for cocaine hydrochloride, phencyclidine hydrochloride, and d-amphetamine sulfate in that order. The doses of each drug were tested in a mixed order. The drugs were dissolved in saline and injected intramuscularly (gluteus m.) 5 min presession. Drug sessions were separated by at least five days, during



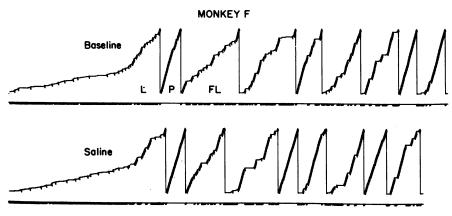


Fig. 2. Cumulative response records for both baseline and saline sessions for each subject responding under a multiple schedule with learning (L), performance (P), and faded-learning (FL) components. The response pen stepped upward with each correct response and was deflected downward each time the four-response sequence was completed. Errors are indicated by the event pen, which was held down during each timeout. A change in components of the multiple schedule reset the stepping pen. The event pen was also displaced downward during the delay that separated a component change.

which time there were baseline sessions and a control session (saline alone injected intramuscularly 5 min presession). The volume of each injection was .05 ml/kg body weight.

RESULTS

Cumulative response records for representative baseline sessions for each subject are shown in Figure 2. The response pen stepped with each correct response and was deflected downward each time the four-response sequence was completed. Errors are indicated by the event pen, which was held down during each timeout. The event pen was also deflected and the response pen reset with each component change. As is shown in the baseline record for Monkey C, the session began in the learning component (L), then changed to the performance component (P), which was then followed by the faded-learning component (FL). This order (L-P-FL) was the same throughout the session. Notice that the greatest number of errors (event pen) occurred in the learning component and the fewest in the performance component. Although errors decreased as the session progressed in both the learning and faded-learning components, fewer errors were made in acquiring the sequence with the fading procedure. By the end of the session (last three excursions of the response pen), the behavior in each of the three components was virtually identical in terms of both errors and rates of correct responding. The baseline behavior of Monkey F was similar, though the error levels in both of the acquisition components were higher for this subject than for Monkey C. A representative record for a session that was preceded by the administration of saline is also shown for each subject in Figure 2. Generally, both the total errors and the patterns of within-session error reduction (acquisition) following saline administration were comparable to those observed under baseline conditions for each subject.

d-Amphetamine dose-effect curves are shown for each subject in Figure 3. The mean and range of 11 saline control sessions (C) are shown at the left of each curve. Generally, damphetamine decreased response rate in both acquisition components as a function of increasing doses. For Monkey C, however, response rate in the learning component increased at low doses (.18 and .32 mg/kg). In

the performance component, response rate increased in Monkey C across a range of doses (.18 to .56 mg/kg), while for Monkey F these same doses had no effect. In each subject, response rate in the performance component decreased only at the highest dose (1 mg/kg). In all three components, percent errors tended to increase as a function of increasing doses of d-amphetamine. However, large error-increasing effects occurred in the learning component at doses that had little or no effect on errors in the faded-learning and performance components (e.g., Monkey C, .32 mg/kg; Monkey F, .32 and .42 mg/kg). Finally, it should be noted that with a single exception (Monkey C, .32 mg/kg), whenever errors increased in an acquisition component, response rate in that same component decreased.

The effects of d-amphetamine on acquisition in both the learning and faded-learning components can be seen in the cumulative records for Monkey C shown in Figure 4. In comparison to saline (Figure 2) the major effect of the .32 mg/kg dose (top record) was to increase errors in the learning (L) component during the first cycle of the multiple schedule. Though errors occurred throughout the session in both learning and faded-learning components, acquisition of both response sequences was evident by the end of the session. The effects of d-amphetamine on acquisition were more pronounced at the .56 mg/kg dose (lower records). The largest effect occurred in the learning component and acquisition of the response sequence did not occur in this component until the third cycle of the multiple schedule. Note that errors also increased in the faded-learning and performance components during the first and second cycles of the multiple schedule. Long pauses in responding during both the learning and faded-learning components were also apparent at this dose. Such pausing was frequently observed in both subjects at the higher doses of d-amphetamine.

The effects of cocaine on percent errors and rate of responding are shown for each subject in the dose-effect curves of Figure 5. The mean and range of 14 saline control sessions (C) are shown at the left of each curve. Though the control data of Monkey C were somewhat variable, low to intermediate doses of cocaine (.1 to 1 mg/kg) generally had little or no effect on response rate in either subject, whereas higher doses (1.8 to 3.2 mg/kg) decreased re-

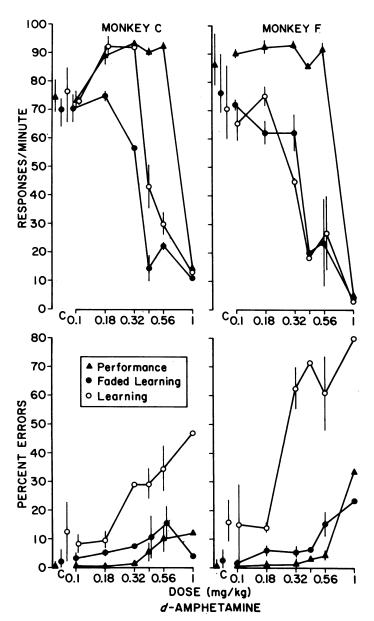


Fig. 3. Effects of varying doses of d-amphetamine on the overall response rate and percent errors in each component of the multiple schedule for each subject. The mean and range (vertical lines) of 11 saline control sessions (C) are shown at the left of each dose-effect curve. For each curve the mean and range (vertical lines) for two determinations are shown. The data points shown without a range represent a single determination at that dose.

sponse rates in each component of the multiple schedule. The effects of cocaine on accuracy (i.e., percent errors) were similar to those obtained with d-amphetamine in both subjects. For Monkey C, errors increased in the learning component but not in the faded-learning or performance components at doses of .56 and 1

mg/kg, while higher doses (1.8 to 3.2 mg/kg) increased errors in all three components of the multiple schedule. Even greater selectivity of drug effect can be seen in the data of Monkey F. At the .32 mg/kg dose, errors were selectively increased in the learning component, while at doses of .56 and 1 mg/kg, errors in-

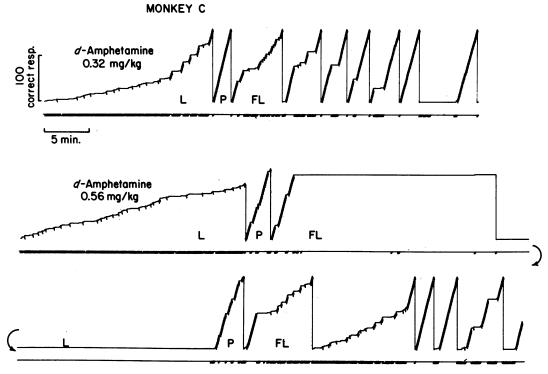


Fig. 4. Within-session effects of two doses of d-amphetamine on the responding of Monkey C under the multiple schedule. The recording details are the same as in Figure 2.

creased in both the learning and fadedlearning components but not in the performance component. As was found with Monkey C, higher doses (1.8 to 3.2 mg/kg) increased errors in all three components. It is interesting to note that, unlike d-amphetamine, certain doses of cocaine increased errors without decreasing response rate (e.g., learning component: .56 mg/kg).

The effects of cocaine on acquisition are shown for Monkey C in Figure 6. The .56 mg/ kg dose (top record) increased errors in the learning component but not in the faded-learning or performance components. Acquisition of the sequence in the learning component was not evident until the end of the second cycle of the multiple schedule, and errors occurred in this component throughout the session. Though the overall error levels did not increase, there was an effect on acquisition in the faded-learning component. Note that at the beginning of the component, which corresponds with the early steps in the fading procedure, several sequences were completed without errors (indicated by the arrow). As the

subject reached the later stages of the fading procedure, the frequency of errors abruptly increased. Thereafter the discriminability (i.e., luminance level) of the stimulus indicating a correct response in each sequence position titrated with the subject's behavior until the sequence was acquired toward the end of the component. During the remainder of the session, few additional errors were made in the faded-learning component. As is shown in the lower records of Figure 6, a higher dose of cocaine (2.4 mg/kg) increased errors in all three components of the multiple schedule. Acquisition in the learning component was virtually eliminated, while in the faded-learning and performance components the disruptive effects of cocaine diminished as the session progressed. Similar to the effects obtained at the lower dose, several sequences were completed at the beginning of the first faded-learning component (indicated by the arrow). The fading procedure, however, did not attenuate the errorincreasing effects produced by the higher dose of cocaine and errors occurred throughout the component. Additionally, as can be readily

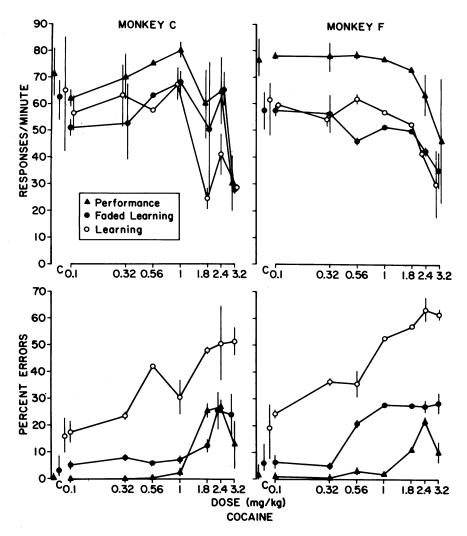


Fig. 5. Effects of varying doses of cocaine on the overall response rate and percent errors in each component of the multiple schedule for each subject. The mean and range (vertical lines) of 14 saline control sessions (C) are shown at the left of each dose-effect curve. For each curve the mean and range (vertical lines) for two determinations are shown. The data points shown without a range represent a single determination at that dose.

seen in the cumulative record, cocaine, unlike d-amphetamine, did not produce long pauses in responding. This was true for both subjects at the higher doses.

Phencyclidine dose-effect curves are shown for each subject in Figure 7. The mean and range of 14 saline control sessions (C) are shown at the left of each curve. No rate-increasing effects were found with phencyclidine at any of the doses tested. In Monkey C, intermediate doses (.1 and .13 mg/kg) decreased response rate in the two acquisition components, whereas higher doses decreased

rate in all three components. The data were similar for Monkey F, though this subject tended to be more sensitive to the rate-decreasing effects of phencyclidine. The .056 mg/kg dose selectively decreased rate in the learning component, while higher doses (.1 to .24 mg/kg) had approximately equivalent rate-decreasing effects in each component of the multiple schedule. Across the range of doses tested, phencyclidine generally produced fewer selective error-increasing effects than did either damphetamine or cocaine. In both subjects only the .056 mg/kg dose selectively increased errors

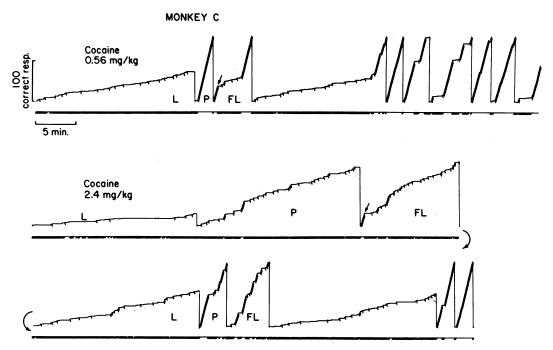


Fig. 6. Within-session effects of two doses of cocaine on the responding of Monkey C under the multiple schedule. The recording details are the same as in Figure 2.

in the learning component. Higher doses (.1 to .24 mg/kg) produced large error-increasing effects in all three components of the multiple schedule. Additionally, with two exceptions (Monkey C: learning, .056 mg/kg and performance, .13 mg/kg), those doses of phencyclidine that increased errors in a particular component also decreased response rate in that same component. This relationship was similar to that obtained with d-amphetamine.

The effects of phencyclidine on acquisition are shown for Monkey C in Figure 8. Though errors were selectively increased in the learning component at the .056 mg/kg dose (top record), the sequence was acquired. The main effect of this dose was to increase errors at the beginning of the session during the first learning component. A short run of errors, however, was also made throughout the session at the start of each learning component. Though errors increased in all three components at the .18 mg/kg dose (lower records), selective effects were evident during the later parts of the session. In the first cycle, errors increased in each component of the multiple schedule. During the second cycle, few errors were made in the performance component, while responding in

the learning and faded-learning components was still disrupted. Finally, during the third cycle, responding continued to be disrupted in the learning component, while virtually no errors were made in the performance component, and errors decreased in the faded-learning component as the subject began to acquire the sequence. Note also that, unlike d-amphetamine (Figure 4) and like cocaine (Figure 6), long pauses in responding were infrequent with phencyclidine at doses that increased errors in all three components of the multiple schedule.

DISCUSSION

The rate-decreasing effects obtained in the present study are consistent with previous reports that d-amphetamine and cocaine decrease the rate of responding under fixed-ratio (FR) schedules of food presentation in monkeys (e.g., Downs & Woods, 1975; Gonzalez & Goldberg, 1977; Johanson, 1978; Kelleher & Morse, 1964; Spealman, Goldberg, Kelleher, Goldberg, & Charlton, 1977; Wilson & Schuster, 1975; Woods & Tessel, 1974). At certain doses both d-amphetamine and cocaine have also

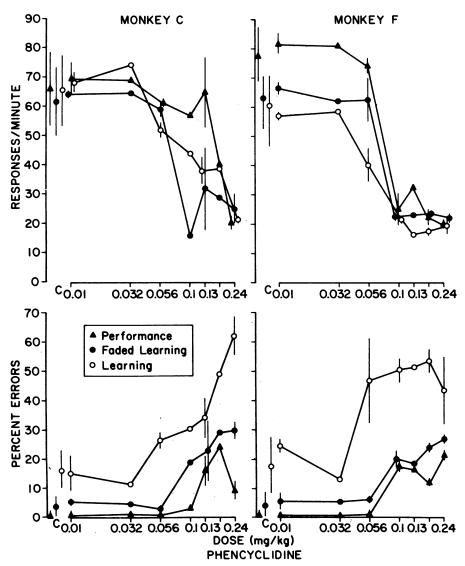


Fig. 7. Effects of varying doses of phencyclidine on the overall response rate and percent errors in each component of the multiple schedule for each subject. The mean and range (vertical lines) of 14 saline control sessions (C) are shown at the left of each dose-effect curve. For each curve, the mean and range (vertical lines) for two determinations are shown. The data points shown without a range represent a single determination at that dose.

been reported to increase the rate of responding maintained under second-order schedules of food presentation (Gonzalez & Goldberg, 1977; Thompson & Moerschbaecher, 1979). For example, Thompson and Moerschbaecher (1979) investigated the effects of d-amphetamine and cocaine on the acquisition and performance of response chains in monkeys. In one component of a multiple schedule of food presentation, the subjects acquired a different four-response chain each session by responding

sequentially on three keys in the presence of four geometric forms (chain learning). In the other component the four-response chain was the same each session (chain performance). In both components every fifth completion of the four-response chain produced a food pellet. At intermediate doses both d-amphetamine and cocaine were found to increase the overall rate of responding in both components in some subjects. Similarly, responding in the present study may be considered to have been

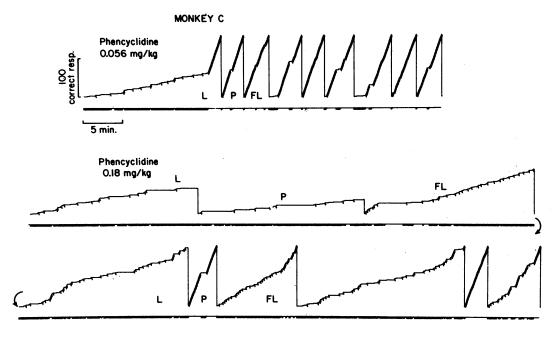


Fig. 8. Within-session effects of two doses of phencyclidine on the responding of Monkey C under the multiple schedule. The recording details are the same as in Figure 2.

maintained under a second-order schedule since a sequence was comprised of four responses and every second completion of the sequence produced food. The rate-increasing effects obtained in one subject with intermediate doses of d-amphetamine (Figure 3, Monkey C) are consistent with the data of Gonzalez and Goldberg (1977) and Thompson and Moerschbaecher (1979).

Phencyclidine has been reported to produce decreases in response rate under FR schedules of food presentation (Balster & Chait, 1976; Chait & Balster, 1978; Wenger, 1976; Wenger & Dews, 1976). For example, Balster and Chait (1976), using rhesus monkeys as subjects, found that phencyclidine at doses ranging from .05 to .20 mg/kg only decreased the rate of responding in the FR component of a chain FI FR schedule. The present results are in agreement with these data and suggest that the patas monkey is sensitive to phencyclidine within a dose range comparable to that reported for the rhesus monkey.

Selective error-increasing effects between components of the multiple schedule were obtained with each of the three drugs tested. Generally, errors increased in the learning component at lower doses than those required to disrupt behavior in the faded-learning component. The performance component tended to be the least sensitive to disruptive drug effects. Errors in the performance component were increased either at comparable or slightly higher doses than those which increased errors in the faded-learning component. The selective error-increasing effects of d-amphetamine and cocaine are similar to those previously obtained on both simple and multiple schedules of repeated acquisition and performance of behavioral chains (e.g., Moerschbaecher et al., 1979; Thompson, 1974, 1977; Thompson & Moerschbaecher, 1979). For example, in the Thompson and Moerschbaecher (1979) study, both d-amphetamine and cocaine were found to increase errors in the learning component at doses that had no effect on errors in the performance component. In that study each of the four responses in the sequence was associated with a different discriminative stimulus; i.e., a chain schedule was used. In the present study, however, there was no such stimulus change; i.e., a tandem schedule was used. The present data therefore extend earlier findings (Moerschbaecher et al., 1979; Thompson & Moerschbaecher, 1979) of selective drug effects between chain learning and performance to a tandem schedule. In addition the data indicate that the effects of phencyclidine on the acquisition of a complex discrimination are similar to those of d-amphetamine and cocaine.

The degree to which behavior is under stimulus control is one proposed mechanism by which selective drug effects, such as those obtained in the present study, may be explained (Laties, 1975; Thompson, 1978). Variations in stimulus control may function to modulate drug action, such that behavior under strong control by discriminative stimuli is less affected by drugs than behavior under weak control by discriminative stimuli. In the present study relatively strong stimulus control was indicated by the low baseline error levels in the performance component. The behavior in this same component was found to be the least sensitive to the disruptive effects of the drugs.

Certain doses of each of the three drugs tested were found to increase errors in the learning component but not in the faded-learning component. These results demonstrate that the use of a fading procedure may function to attenuate the error-increasing effects of a drug on an acquisition baseline. It has been suggested that differences in the rate of reinforcement between components of a multiple schedule may influence a drug's acute effects (Moerschbaecher et al., 1979). In the learning component the rate of reinforcement decreased as errors increased. This was not the case, however, in the faded-learning component. In the faded-learning component, the discriminability of the stimulus indicating a correct response adjusted as a function of the subject's behavior. As errors occurred the discrimination became less difficult and the reinforced sequence of responding was generally reinstated. The maintenance of a high rate of reinforcement might therefore be one mechanism by which a fading procedure may modulate the effects of drugs on acquisition.

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